Laboratory Science and Biological Markers of Cardiovascular Disease

GW25-e3246

Expressions of tnfsf6 and cyp1a1 and screening related genes by GeneChip on peripheral blood mononuclear cells in patients with Acute Myocardial Infarction

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Objectives: Understand the changes in the genes of oxidative stress and the process of cell toxic with myocardial IRI due to before and after operative of PCI in STEMI patients. Observe in a dynamic environment the changes in the mRNA expression of TNFSF6 and CYP1A1 resulting from myocardial IRI and clinical significance.
Methods: Patients admitted to our ER and CCU from November 2011to February 2012. Consisting of 22 patients, 14 males and 8 females, mean age 63.52±12.40 years with a range from 37 to 91years. All cases are diagnosed based on the AMI diagnosis criteria under Chinese Medical Association in 2003, For patients with normal controls with age, sex matching healthy volunteers 12 people, 8 male and 4 female, the average age 57.00±6.57 (35-68). Acute onset in STEMI group hospital diagnosed after extracting cubits 10ml were immediately into containing 0.05 ml of heparin without bacteria. After acute onset of emergency PCI and conventional treatment, the third day and the seventh day each pump once again were cubits 10ml; The comparison group: morning, fasting extraction method 10ml were cubits under the same approach as that for the patients group. PBMCs separation adopts the lymphocyte separate liquid density gradient centrifugation. Using Human Stress & Toxicity Pathway Finder PCR Array screening method of myocardial IRI related gene changes. The validation of expression of CYP1A1 TNFSF6 by Real time PCR. All data to differences with mean±standard deviation (x±s), Value of patients and controls were compared by ANOVA analysis. And correlation analysis method, the related to $P<0.05$ to was statistically significant differences.
Results: (1) Of the STEMI group, general average STEMI genes that significant changes in 14, which were up regulated the gene expression of significant for 8, were significant down regulated for four genes.The genes expression were up regulated which are cell growth/aging related genes1 (GADD45A), oxidation stress and metabolic related gene 1 (PRDX2), Heat shock related gene 3 (HSPD1, DNAJB1, DNAJB2), and repair DNA damage related gene 1 (RAD50), and apoptosis signal related gene 2 (TNFSF6 TRADD,) Significant down regulated of those genes: the cell proliferation/cancer related gene 1 (CCNG1), oxidation or metabolic stress related gene gene 2 (CAT, CYP1A1), DNA damage and restoration related gene 1 (ATM). (2) The expression of TNFSF6 in STEMI group is higher than of the healthy group and CYP1A1 was lower than the normal value.
Conclusions: (1) The moderation of multiple genes resulting from myocardial IRI due to After PCI with Acute myocardial infarction. It provides a more complete view in the complication and complexity of myocardial IRI gene regulation. (2) The quantitative analysis of TNFSF 6 and CYP1A1 genes after myocardial IRI in AMI at various stage. They may be involved in the myocardial ischemia/ reperfusion injury physiopathological process.

GW25-e1618

Analysis of Bacteroides and Bifidobacterium diversity in fecal samples from patients with coronary artery disease by using PCR-denaturing gradient gel electrophoresis fingerprint

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Objectives: The investigation provides molecular analyses of the faecal microbiota in coronary artery disease (CAD). This study aimed to clarify the relationship between CAD and gut predominant microbiota by analyzing the diversity of Bacteroides and Bifidobacterium.
Methods: In order to assess whether there are changes in the diversity and similarity of gut microbiota in CAD patients when compared with healthy individuals, bacterial DNAs from 30 CAD and 30 healthy individuals were extracted from faecal samples and characterised by PCR-denaturing gradient gel electrophoresis (DGGE) with primers specifically targeting V3 region of the 16S rRNA gene. After DGGE profilings was obtained, the diversity and similarity analyses were carried out by the number of band, Shannon-Weaver (Hp), cluster analysis and the cumulative distribution curve of similarity.
Results: The range of Shannon-Weaver (Hp) in diabetes group and healthy group was 0. 88 (0.74-0.94) and 0. 94 (0.88-0.96) for Bacteroides; 0.84 (0.74-0.93) and 0. 87 (0.73-0.93) for Bifidobacterium. The cumulative distribution curve of intra-group similarity showed that the Dice similarity coefficient (Cs) lower than (or equal to) 0.5 took up 85. 83% of the total Cs for Bacteroides in diabetes group and 35.71% in healthy group; the Cs lower than (or equal to) 0.4 constituted 90% of the total Cs for Bifidobacterium in CAD group and 60.7% in healthy group. It is showed that the composition of gut microbiota in CAD group might be changed due to atherosclerosis status.
Conclusions: Sequencing results also revealed that bacterial composition of CAD group was different from that of the healthy group. DGGE profiling has shown individual specificity in CAD group and healthy group for Bacteroides and Bifidobacterium. The intra-group similarity of Bacteroides and Bifidobacterium is lower in CAD group than in healthy group. Taken together, in this work we observed the characterisation of gut microbiota in CAD patients, which suggestes that the gut microbiota of CAD patients have some changes associated with occurrence and development of CAD.

GW25-e3093

Predictive value of serum uric acid level for left atrial thrombus or spontaneous echo contrast in patients with atrial fibrillation

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Objectives: To investigate the predictive value of serum uric acid (SUA) levels for left atrial thrombus (LATH)/spontaneous echo contrast (SEC) in patients with atrial fibrillation (AF).
Methods: The study enrolled 525 patients (Male 337, Female 188, mean age of 60.8±11.2 years old, 83% paroxysmal AF) with AF who underwent transesophageal echocardiography (TEE) in Guangdong province cardiovascular institute from July 2007 to January 2013. Patients were categorized into LATH/SEC group (n=57) and non-LATH/SEC group (n=468), according to the TEE results. The clinical baseline of both groups including age, gender, AF types, SUA levels, indices of echocardiography and complications were collected and analyzed. The relationships between the potential risk factors and LATH/SEC were performance using Logistic regression analysis.
Results: SUA level (391.63±98.45umol/L vs 349.27±83.93 umol/L, $P<0.01$), left atrial diameter (LAD) (41.95±6.06mm vs 37.44±5.17mm, $P<0.01$), proportion of patients with persistent AF (50.9% vs 13.7%, $P<0.01$) were significantly increased in patients of LATH/SEC group compared with patients of non-LATH/SEC group. ROC curve were presented by SUA level, which indicated area under curve was 0.612 ($P=0.006$) and the best SUA cut-point was 448.5umol/L. Logistic regression analysis indicated that female (OR=2.344, 95% CI 1.228-4.475, $P=0.01$), persistent AF (OR=5.993, 95% CI 3.127-11.486, $P<0.001$), SUA level (OR=2.890, 95% CI 1.380-6.051, $P=0.005$), LAD>40mm (OR=4.845, 95% CI 2.528-9.284, $P<0.001$), CHA2DS2-VASc score (OR=1.422, 95% CI 1.105-1.829, $P=0.006$) were independent risk factors of LATH/SEC in patients with AF.
Conclusions: SUA level is independent risk factor and predictive index for LATH/SEC in patients with AF.

GW25-e3529

Traditional Chinese Medication Qiliqiangxin attenuates cardiac remodeling after acute myocardial infarction in mice

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Objectives: Qiliqiangxin (QL), a traditional Chinese medicine, has been approved by China Food and Drug Administration for the treatment of chronic heart failure since 2004. Recently, a multicenter randomized double-blind study from our group has proved that QL reduced the levels of B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) during 12 weeks of treatment in 512 chronic heart failure patients, suggesting that QL may have a protective effect on injury heart. However, whether QL can improve cardiac remodeling and the underling mechanism are still unclear.
Methods: Four groups of C57BL/6 adult male mice (saline plus sham, saline plus AMI remodeling, QL (0.5g/kg/d) plus sham, and QL (0.5g/kg/d) plus AMI remodeling) were randomly divided in this study. Echocardiography and histopathology were detected to evalute cardiac function and morphological changes. TTC staining and immunofluorescence were used to test myocardial necrosis and apoptosis. Quantitative reverse transcription polymerase chain reactions (RT-PCRs) and western blotting were also used to determine the expression levels of peroxisome proliferator-activated receptor-α (PPAR-α), -β, - γ.
Results: QL significantly prevented AMI-induced decreases in ejection fraction (% EF: MI with saline 38%, MI with QL 48%) and fractional shortening (%FS: MI with saline 18%, MI with QL 22%) after AMI. In addition, QL decreased myocardial infarct size by 49% and myocardial apoptosis by 40%. Most imoprtantly, PPARγ, a key regulator for cardiac energy metabolism after myocardial injury, was found to be down-regulated in AMI remodeling and was up-regulated after QL administration. A selective PPARγ activator Rosiglitazone (at a dose of 1mg/kg/d for 21 days via intraperitoneal injection) itself had a protective effect on cardiac function after AMI remodeling. Compared with the administration of QL alone, combination of PPARγ activator with QL did not have significant difference on cardiac function

after AMI remodeling. Importantly, a selective PPARγ inhibitor T0070907 (at a dose of 1 mg/kg/g for 21 days) prevented the protective effects of QL against AMI remodeling. Cardiac function were decreased after the combination of PPARγ inhibitor with QL. Myocardial infarct size and apoptosis-related factors were all increased, confiming the inhibition effect of PPARγ inhibitor on QL. Thses results indicated that QL attenuates cardiac remodeling after AMI through PPARγ. To further claify whether QL takes effetcs in acute stage or remodeling stage, mice was either treated for 3 days or from 3 days-21days. It is found that QL performed functional effect mainly during chronic stage, and had no evident effect on acute stage as determined by measuring the percentage of myocardial ischemic infarct size/area-at-risk (AAR).
Conclusions: QL attenuates cardiac remodeling after AMI. The effects of QL in attenuating cardiac remodeling after AMI was at least partially via targeting PPARγ.

GW25-e5193

The remodeling of gallbladder artery and altered expression of calcium handling genes in hypertensive patients

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Objectives: The remodeling of gallbladder artery in hypertensive patients and its underlying mechanisms are poorly understood. The present study observed the morphological and histological changes of gallbladder arteries and investigated the mechanisms of calcium handling genes involved in remodeling.
Methods: A total of 44 patients with biliary calculus underwent cholecystectomy at department of hepatobiliary surgery in Affiliated Hospital of Zunyi Medical College from Jun, 2011 to Mar, 2012. Among them, 21 patients without risk factors were selected on age and sex-matched method and divided into control group (n=11, normal blood pressure) and hypertensive group (n=10). HE staining and Masson staining were used to observe the morphology changes of arteries. The intima-media thickness (IMT), intimal cross-sectional area (ICSA), medial cross-sectional area (MCSA), collagen volume fraction (CVF) of intima and media was analyzed by computer image analysis system. The protein expressions of α-smooth muscle actin (α-SMA) and proliferating cell nuclear antigen (PCNA) were detected by immunohistochemical technique. The mRNA expression levels of embryonic smooth muscle myosin heavy chain (SMemb) and calcium handling genes were detected by Realtime PCR.
Results: Compared with control group, IMT (79.5±4.7 vs 51.2±4.3 μm), intima-media thickness to internal diameter ratio (IMT/ID) (0.25±0.02 vs 0.17±0.01), ICSA to internal diameter ratio (ICSA/ID) (67.7±9.2 vs 39.6±8.7) and MCSA to ID ratio (MCSA/ID) (242.4±20.7 vs 153.3±19.7) were increased in hypertensive group (all $P<0.05$); Compared with control group, in intima or media of artery, CVF (0.36±0.03 vs 0.17±0.03; 0.36±0.02 vs 0.28 ±0.02, all $P<0.05$) and cell proliferation index (0.61±0.05 vs 0.36±0.05; 0.73±0.05 vs 0.54±0.05, all $P<0.01$) were increased in hypertension subjects; In media of artery, the gene expression of SMemb, sodium pump α_1 subunit and transient receptor potential canonical channel type 1 (TRPC1), TRPC3 were increased, while sodium pump α_3 subunit and plasma membrane calcium-transporting ATPase 4 were decreased in hypertensive group (all $P<0.05$).
Conclusions: This study provides evidences that hypertension is associated with the remodeling of the gallbladder artery. The phenotypic change of vascular smooth muscle cell and the abnormal expression of the calcium handling genes may play an important role in the arterial remodeling.

GW25-e1736

The role of neutrophil-lymphocyte ratio in Takayasu arteritis disease monitoring

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Objectives: Blood neutrophil-lymphocyte ratio (NLR) is an indicator of the overall inflammatory status of the body. Takayasu arteritis (TA) is a chronic non-specific inflammatory disease. The objective of the present study was to assess whether the NLR would be useful in TA disease monitoring. Additionally, a possible relationship between NLR and other inflammatory markers in patients with TA was also investigated.
Methods: Eighty-seven patients and 59 healthy controls were enrolled in the study. The neutrophil and lymphocyte counts were recorded, and the NLR was calculated from these parameters. Disease activity and severity in patients with TA were defined according to the National Institutes of Health and Ishikawa's criteria, respectively.
Results: NLR values were higher in patients with TA compared with healthy controls [2.02 (1.68-3.00) vs. 1.70 (1.37-2.16), $P<0.001$]. There were also significant differences in the NLR values between patients with active disease and patients in remission [2.63 (1.95-4.13) vs. 1.81 (1.50-2.38), $P<0.001$]. Patients with severe TA showed significantly higher NLR values than those with mild-moderate TA [2.09 (1.74-4.20) vs. 1.94 (1.64-2.68), $P=0.033$]. In patients with available longitudinal data, NLR values at the active phase were significantly higher than those at the stable phase [2.86 (2.28-4.84) vs. 2.13 (1.51-3.14), $P=0.001$]. Moreover, NLR values were found to be correlated with inflammatory markers, including C-reactive protein ($\rho= 0.262$, $P=0.014$), erythrocyte sedimentation rate ($\rho = 0.255$, $P=0.017$), and white blood cell count ($\rho = 0.429$, $P<0.001$).
Conclusions: NLR values were significantly increased in patients with active TA exhibiting severe complications. These results indicated that NLR may be a useful marker to assess disease activity, severity, and progression of TA.

GW25-e0290

Pharmacologic approach to defective protein trafficking in the E637K-hERG mutant with PD-118057 and thapsigargin

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Objectives: Treatment of LQT2 is inadequate. Many drugs which can pharmacologically rescue defective protein trafficking in LQT2 also result in potent blockade of HERG current, negating their therapeutic benefit. It is reported that PD-118057 and thapsigargin can rescue LQT2 without hERG channel blockade, but the precise mechanism of action is unknown. Furthermore, the effect of PD-118057 and thapsigargin on the dominant negative E637K-hERG mutant has not been previously investigated.
Methods: The whole-cell Patch-clamp technique was used to assess the effect of PD-118057 and thapsigargin on the electrophysiological characteristics of the rapidly activating delayed rectifier K^+ current (I_{kr}) of the hERG protein channel.Western blot was done to investigate pharmacological rescue on hERG protein channel function.
Results: In our study, PD-118057 was shown to significantly enhance both the maximum current amplitude and tail current amplitude, but did not alter the gating and kinetic properties of the WT-hERG channel, with the exception of accelerating steady-state inactivation. Additionally, thapsigargin shows a similar result as PD-118057 for the WT-hERG channel, but with the exception of attenuating steady-state inactivation. However, for the WT/E637K-hERG channel, PD-118057 had no effect on either the current or on the gating and kinetic properties. Furthermore, thapsigargin treatment did not alter the current or the gating and kinetic properties of the WT/E637K-hERG channel, with the exception of opening at more positive voltages.
Conclusions: Our findings illustrate that neither PD-118057 nor thapsigargin play a role in correcting the dominant-negative effect of the E637K-hERG mutant.

GW25-e4298

Frequency of Hyponatremia and Short Term Clinical Outcomes in Patients Hospitalized for Heart Failure

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Objectives: The objective of this study was to determine the frequency of hyponatremia and short term clinical outcomes in patients hospitalized for heart failure.
Methods: This study was carried out from August 9, 2011, to July 29, 2012. Both male and female patients aged 14 years and above admitted for heart failure fulfilling the inclusion criteria, were included in the study. Admission Serum sodium was measured in all patients. Those having serum sodium of ≤135mmol/L were defined as hyponatremic. All the patients were managed according to guidelines. All patients were followed during their hospital stay. Patients who survived were discharged on standard HF medications and followed till the end of six month for 6-month mortality and re-admissions for heart failure.
Results: A total of 241 patients were included in the study. Mean age was 59.2±14.9 (18-100) years. The number of female patients was 123 (51%) while male were 118 (49%). Based on age patients were divided into two groups, Group I included patients less than 60 years (41.9%, n-101)and Group II included 60 years and above (58.1% (n-140). Mean serum sodium was 136±5.1mmol/L (116-151). Hyponatremia (serum sodium ≤135mmol/L) was found in 35.3% (85) patients. The overall in-hospital mortality rate was 5.4%. Lower admission serum sodium was associated with higher in-hospital mortality, 8.2% for the lower sodium group compared with 3.8% for those patients with normal serum sodium ($P=0.23$). Mean length of hospital stay (LOS) for overall CHF patients was 3.8±2.4 days. Lower admission serum sodium was associated with longer mean hospital LOS, 4.1±2.3 for lower sodium group compared with 3.7±2.4 for normonatremic group. Overall 6-month follow up mortality was 19.6%, while it was higher in hyponatremic group 28.0% compared to normonatremic patients 15.3% ($P=0.03$). Six month follow up readmission rate was 30.7%. Hyponatremic group had readmission rate of 34.7% compared with 28.7% in normonatremic patients ($P=0.36$).
Conclusions: Hyponatremia in hospitalized patients with heart failure is common and is associated with longer hospital stay, higher in-hospital and early post-discharge mortality.

GW25-e4585

Effects of CD147/MMP-2 Pathway on Early Left Ventricular Remodeling in Spontaneously Hypertensive Rats

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